27. (Amended) A nucleic acid sequence capable of hybridizing under stringency conditions of 0.2-1.0 × SSPE, 0.1% SDS, 50° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching, to at least one member of the group consisting of SEQ ID Nos. 1, 2, 5 and 7,

A3

wherein said nucleic acid sequence is suitably labeled as a probe to identify a receptor sequence having a homology of at least 30% with a member of the group consisting of SEQ ID Nos. 1, 2, 5 and 7, and comprises at least 10 nucleic acid residues.

REMARKS

Entry of this amendment is respectfully requested. No new matter is added by the amendment, because the amended application is fully supported by the application as filed.

The amendments to the specification add the references to the SEQ IDs to the Description of the Figures, as requested by the Examiner; while the amendments to claims 1-8 and 25-27 clarify the intended scope of these claims.

Claims 1-42 are in this application, no claims having been canceled or added, and claims 1-8 and 25-27 having been amended by this amendment.

Claims 9, 16-24, and 28-42 stand withdrawn from consideration.

The specification was objected to; and claims 1-8, 10-15, and 25-27 were rejected under 35 USC 101, 35 USC 102(b), and/or 35 USC 112, ¶¶1 and/or 2. The objection and rejections are respectfully traversed in view of the amendment.

The objection to the specification

The specification was objected to for lack of a reference in either the Description of the Figures or in the figures themselves to the SEQ IDs shown in those figures. The Description of the Figures has been amended to include the relevant SEQ ID for each Figure; and withdrawal of the objection is requested.

The 35 USC 112, ¶2 rejection

Claims 1-8 and 25-27 were rejected under 35 USC 112, ¶2, for indefiniteness for a number of reasons set out in detail in the Office Action ("sequences" and "stringent conditions" in claims 1, 2, 4-8 and 25-27; "comprising" in claim 3, "encoded protein" in claims 6-8, and "related" in claims 25-27), with the Examiner suggesting certain changes to meet the rejections.

The Examiner's helpful suggestions for claim amendments have been adopted, and it is believed that the claims are now definite. With regard to the term "homology", Applicants submit that the term is well understood by those in the art and requires no further explanation for definiteness: measurements of "percent homology" between sequences are given by programs in the commercially-available Vector NTI package, and BLAST, a program from the NCBI and freely available, also gives measurements of homology. Withdrawal of the rejection is requested.

The 35 USC 101 and 35 USC 112, ¶1, utility rejection

Claims 1-8, 10-15, and 25-27 were rejected under 35 USC 101 for lack of utility and also under 35 USC 112, ¶1, for lack of "how to use" description because of that lack of utility. These rejections, as applied to the amended claims, are respectfully traversed.

The application describes the phenomenon of "pheromones", small volatile molecules that mediate chemical communication between animals. Pheromones as such are well understood in the dealing with the insect world, for example, where a pheromone from the female of a given insect species, used by the female in nature to attract a male of the species, may be synthetically prepared and used as a bait in a trap for the males of the species (e.g. Gossyplure®). Moths, for example, detect pheromones through specialized cells in their antennae. Vertebrates are described as possessing an organ within the nasal cavity, the vomeronasal organ, that is adapted for the detection of pheromones.

Research on humans has established the existence of the human vomeronasal organ, and its connection to the brain, and established that its tissue is distinct from normal olfactory tissue and that its connection to the brain is different from that of olfactory tissue. This research has also established the existence of human pheromones, referred to by the assignee as "vomeropherins", that through interaction with the vomeronasal organ can cause both physiological and psychological changes in humans exposed to them; and that these changes are mediated through receptors in vomeronasal epithelial cells. Extensive research by the assignee has established that a number of steroidal vomeropherins cause quite specific physiological and psychological responses in humans exposed to them; and the results of this research have been widely published and are the subject of numerous patents and patent applications. For example, International Application Publication No. WO 01/49280 discloses that certain pregnanes, such as (17β)19-norpregna-1,3,5(10)-trien-3-ol, act to promote weight in humans by interaction with the VNO; and International Application Publication No. WO 01/56577 discloses that certain estranes, such as estra-1,3,5(10),16-tetraen-3-yl acetate, act to increase alertness in humans by interaction with the VNO. The connection between vomeropherins, receptors in the human VNO, and the physiological/psychological effect of the vomeropherins is well established.

The use of receptor-based assays to identify prospective drug candidates is well understood in the field of drug discovery and development. Though it is recognized that not every compound interacting with a receptor will prove to be a useful therapeutic agent, it is equally recognized that the use of receptor assays is a rapid and inexpensive way to identify compounds that are at least potential therapeutic agents and distinguish them from compounds that are not, and to determine which of the compounds has the greatest activity (interaction) with the receptor and therefore the greatest potential therapeutic activity.

It is therefore recognized to be of specific, substantial, and well-established utility to identify receptors and the ligands interacting with them so that these receptors may be used to identify further ligands potentially developable as human therapeutic agents. In this application, there is established the identification of human VNO receptor DNA, and the receptor proteins encoded by that receptor; and Applicants submit that a person of ordinary skill in the art, having regard to that skill and the knowledge of the art, and the disclosure of this application, would immediately contemplate the use of the identified nucleic acids and receptor proteins in the identification and characterization of known existing vomeropherins and the discovery of new vomeropherins, so that the utility requirement of 35 USC 101 and the "how to use" requirement of 35 USC 112, ¶1, is satisfied.

With regard to the Examiner's comments on the range of compounds claimed, e.g. the range of polynucleotides encoding variants of the polypeptide of SEQ ID NO: 3, Applicants submit that the range of polynucleotides and variants is not so great as to lead a person of ordinary skill in the art to consider that such range is overly broad or that such compounds may not be made and used by a person of ordinary skill in the art without undue experimentation. With regard to the Examiner's comments on "fragments", the claims have been amended to require that the variant polynucleotides hybridize to the full length polynucleotides encoding, e.g., SEQ ID NO: 3. With regard to the Examiner's comments on the lack of working examples, Applicants submit that the state of the art on the generation of vectors from polynucleotides is such that a person of ordinary skill in the art with the disclosure of the application would be able to prepare such vectors without undue experimentation, and would have been able to do so at the time of filing of the application, so that the applicants should be considered to have been in possession of the claimed vectors.

Withdrawal of the rejections is requested.

The 35 USC 112, ¶1, written description rejection

Claims 1, 2, 3-15 and 25-27 (*sic*, claims 1-8, 10-15, and 25-27) were rejected under 35 USC 112, ¶1, for a failure of the "written description" requirement. This rejection, as applied to the amended claims, is respectfully traversed.

The Examiner asserts that while the specification discloses a polynucleotide of SEQ ID NO: 1 and two variants, the claims encompass "a vast genus of polynucleotides not described in the specification". The claims have been amended to limit the polynucleotides to those that, for example, have named sequences (e.g. claim 3), or have either named sequences or sequences that hybridize to such sequences (e.g. claims 4, 5, and 27), or have either sequences that encode named proteins or sequences that hybridize to such sequences (e.g. claims 1, 2, 25, and 26), or expression vectors containing such sequences. Such sequences, if not named per se, are described in such a way (as by either the encoded protein or by the sequence to which they hybridize and the conditions for the hybridization) that a person of ordinary skill in the art would readily conceive such sequences from the information given in the application. Applicants submit that the specification provides "written description" support for the claims as amended, and withdrawal of the rejection is requested.

The 35 USC 102(b) rejection

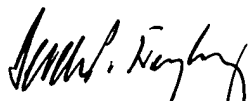
Claim 3 was rejected under 35 USC 102(b) as being anticipated by Saito et al., with the Examiner noting that because the claim recited a cDNA "comprising" certain sequences it encompassed any cDNA, including the cDNA disclosed by Saito et al. and suggesting amendment from "comprising" to "consisting of" would obviate the rejection.

The Examiner's helpful suggestion has been adopted since it also resolves the 35 USC 112, ¶2, rejection of claim 3 discussed above, and it is believed that the claim is now free of anticipation. Withdrawal of the rejection is requested.

Conclusion

Entry of the amendment, and allowance of claims 1-8, 10-15, and 25-27, are respectfully requested.

Respectfully submitted,



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Amended text showing amendments (additions in bold, deletions in strikethrough)

Specification (page 12, line 18 - page 13, line 3)

Figure 1 is the nucleotide sequence of hVNO-R1, **SEQ ID NO: 1**.

Figure 2 is the long form amino acid sequence of hVNO-R1, **SEQ ID NO: 3**. This form of hVNO-R1 ~~hNVO-R1~~ is translated using the first in-frame start codon.

Figure 3 is the short form amino acid sequence of hVNO-R1, **SEQ ID NO: 4**. This form of hVNO-R1 ~~hNVO-R1~~ is translated using the second in-frame start codon.

Figure 4 is the long form amino acid sequence of hVNO-R1, **SEQ ID NO: 4,** with the seven theoretical transmembrane domains indicated.

Figure 5 is the nucleotide sequence of the mutant hVNO-R1 allele, **SEQ ID NO: 5**.

Claims 1-8 and 25-27

1. (Amended) An mRNA ~~and sequences which hybridize thereto under stringent conditions~~ that **encodes a** ~~encode~~ VNO receptor protein ~~or fragment thereof~~ selected from the group consisting of SEQ ID Nos. 3, 4, and 6,
or a polynucleotide that hybridizes thereto under stringency conditions of 0.1 × SSPE, 0.1% SDS, 65° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching.

2. (Amended) A cDNA ~~and sequences which hybridize thereto under stringent conditions~~ that **encodes a** ~~encode~~ VNO receptor protein ~~or fragment thereof~~ selected from the group consisting of SEQ ID Nos. 3, 4, and 6,
or a polynucleotide that hybridizes thereto under stringency conditions of 0.1 × SSPE, 0.1% SDS, 65° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching.

3. (Amended) A cDNA selected from the group **consisting of** ~~comprising~~ SEQ ID Nos. 1, 2, 5 and 7.

4. (Amended) A cDNA ~~and sequences which hybridize thereto under stringent conditions~~ comprising residues 17-1088 of SEQ ID No. 1**, or a polynucleotide that hybridizes thereto under stringency conditions of 0.1 × SSPE, 0.1% SDS, 65° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching.**

5. (Amended) A cDNA ~~and sequences which hybridize thereto under stringent conditions~~ comprising residues 44-1088 of SEQ ID No. 1, **or a polynucleotide that hybridizes thereto under stringency conditions of 0.1 × SSPE, 0.1% SDS, 65° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching.**

6. (Amended) An expression vector,

comprising a cDNA ~~and sequences which hybridize thereto under stringent conditions~~ that **encodes a** ~~encode~~ VNO receptor protein ~~or fragment thereof~~ selected from the group consisting of SEQ ID Nos. 3, 4, and 6, **or a polynucleotide that hybridizes thereto under stringency conditions of 0.1 × SSPE, 0.1% SDS, 65° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching,**

wherein said vector is capable of expressing the ~~encoded~~ protein **encoded by said cDNA or polynucleotide** when introduced into a competent host cell.

7. (Amended) An expression vector,

comprising a cDNA ~~and sequences which hybridize thereto under stringent conditions~~ comprising residues 17-1088 of SEQ ID No. 1, **or a polynucleotide that hybridizes thereto under stringency conditions of 0.1 × SSPE, 0.1% SDS, 65° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching,**

wherein said vector is capable of expressing the ~~encoded~~ protein **encoded by said cDNA or polynucleotide** when introduced into a competent host cell.

8. (Amended) An expression vector,

comprising a cDNA ~~and sequences which hybridize thereto under stringent conditions~~ comprising residues 44-1088 of SEQ ID No. 1, **or a polynucleotide that hybridizes thereto under stringency conditions of 0.1 × SSPE, 0.1% SDS, 65° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching,**

wherein said vector is capable of expressing the ~~encoded~~ protein **encoded by said cDNA or polynucleotide** when introduced into a competent host cell.

25. (Amended) An RNA sequence ~~and sequences which hybridize thereto under stringent conditions~~ that **encodes** ~~encode~~ a VNO receptor protein ~~or fragment thereof~~ selected from the group consisting of SEQ ID Nos. 3, 4 and 6, **or a polynucleotide that hybridizes thereto under stringency conditions of 0.1 × SSPE, 0.1% SDS, 65° C, or a combination of salt, temperature,**

and other reagents that results in selection of the same degree of matching,
suitably labeled as a probe to identify a nucleic acid sequence encoding **a** ~~related~~ pheromone **receptor** ~~receptors~~ **having a homology of at least 30% with a VNO receptor protein selected from the group consisting of SEQ ID Nos. 3, 4 and 6.**

26. (Amended) A DNA sequence ~~and sequences which hybridize thereto under stringent conditions~~ that **encodes** ~~encode~~ a VNO receptor protein ~~or fragment thereof~~ selected from the group consisting of SEQ ID Nos. 3, 4 and 6, **or a polynucleotide that hybridizes thereto under stringency conditions of 0.1 × SSPE, 0.1% SDS, 65° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching,**
suitably labeled as a probe to identify a nucleic acid sequence encoding **a** ~~related~~ pheromone **receptor** ~~receptors~~ **having a homology of at least 30% with a VNO receptor protein selected from the group consisting of SEQ ID Nos. 3, 4 and 6.**

27. (Amended) A nucleic acid sequence capable of hybridizing under ~~low to moderate~~ stringency conditions **of 0.2-1.0 × SSPE, 0.1% SDS, 50° C, or a combination of salt, temperature, and other reagents that results in selection of the same degree of matching,** to at least one member of the group consisting of SEQ ID Nos. 1, 2, 5 and 7,
wherein said nucleic acid sequence is suitably labeled as a probe to identify **a** ~~related~~ receptor **sequence** ~~sequences~~ **having a homology of at least 30% with a member of the group consisting of SEQ ID Nos. 1, 2, 5 and 7,** and comprises at least 10 nucleic acid residues.